

Original article

Beef allergy: a review of 12 cases

Background: Although beef allergy has long been considered a rare condition, the number of studies regarding the nature, epidemiology, and symptoms of beef allergy has been increasing. We aimed to describe the results of allergy work-up of 12 patients who have a convincing history of acute allergic symptoms following beef ingestion.

Methods: Detailed histories of 10 children and two adult relatives were obtained and patients underwent skin prick tests with commercial beef extract, raw beef and cooked beef. Serum total and beef-specific IgE were measured. Labial, and in selected cases, open food challenges were undertaken.

Results: Interestingly, the rate of family history of beef allergy was 67% (8/12). Three patients (two with commercial extract, and one with cooked beef) had positive skin test responses to beef. Ten (83%) patients had elevated serum IgE concentrations (median 316.5 kU/l, range 9–1321 kU/l) and the beef-specific IgE was positive in all patients (median 6.23 kU_A/l, range 0.83–36.6 kU_A/l). Labial food challenge was positive in four (30%) patients. Of the five patients who underwent open food challenges, three were positive and two tolerated the beef administered.

Conclusions: We conclude that skin prick tests do not accurately diagnose IgE-mediated sensitization to beef. Thus, patients with suspected beef allergy should be screened additionally for beef-specific IgE antibodies, and in selected cases oral food challenge should be carried out to verify the diagnosis.

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Key words: beef allergy; beef-specific IgE; labial food challenge; open food challenge; skin prick test; prick–prick skin test.

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Beef is one of the infrequent causes of food allergy, either in childhood, or in adulthood. Studies dealing with the characteristics of beef allergy consist of cases, with a predominance of children, with atopic dermatitis (1–4). On the other hand, acute, life-threatening reactions after meals containing beef have been shown to be caused by antibiotics, particularly penicillin and streptomycin (5, 6).

In this article we described the results of allergy work-up of 12 patients who have a convincing history of acute allergic symptoms following beef ingestion.

Material and methods

Subjects

Ten children (seven males, and three females) admitted or referred with clinical manifestations, such as pruritus, urticaria, angioedema, nausea, vomiting, rhinorrhoea, sneezing, hoarseness, wheezing, and dyspnoea, following beef ingestion during the period of January 1998 to December 2001, were enrolled in the study. The relatives of these patients with a positive history of beef allergy were also invited for evaluation. Two (two males) of five relatives with a positive history accepted for evaluation and the study sample was enlarged to a total of 12 patients. One patient had atopic dermatitis, five had asthma, and four had allergic rhinitis. Nine patients (except patients 6, 9, and 11) explained that they have found lamb repugnant and have been

reluctant to eat lamb. None of the patients reported allergic reactions to chicken, turkey, fish, cow's milk, and any other foods. None of them had penicillin allergy. None of the patients reported symptoms through contact and/or inhalational exposure to beef.

All patients had been diagnosed as beef allergic by local physicians without any allergy work-up, avoidance measures had been recommended, and all were on a strict diet for at least 2 years.

The term anaphylaxis was used to describe a severe, life-threatening, generalized or systemic reaction (7).

All patients had history of several emergency admittances following beef ingestion (steam-cooked, or grilled, or roasted) but none of them required hospitalization. In each patient, clinical presentations of recurrent episodes after beef ingestion were somewhat similar to previous reactions. Symptoms were limited to the skin in four patients (patients 3, 9, 11, and 12). The other eight patients' reactions were uniphasic anaphylaxis with no obvious biphasic or protracted reactions. None of them had a history of circulatory collapse.

The median reported age of onset of beef allergy was 4 (inter quartile ranges, 3; 5) years. The most reported symptoms were urticaria in 11 (92%) and pruritus in nine (75%). The median reported time of onset of symptoms after ingesting beef was one (inter quartile ranges, 0.25; 1) hour.

Patient 6 was father of patient 5, and patient 9 was father of patients 7 and 8, and uncle of patient 10. Patients 4 and 11 also reported beef allergic relatives. All patients came from two adjacent cities in the eastern Black Sea region of Turkey (nine from Giresun, and three from Ordu). Patient profiles can be seen in Table 1.

Table 1. Patient profiles

Patient no.	Age (years)	Sex	History	Reported age of beef allergy (years)	Reported symptoms after ingesting beef	Reported time of onset of symptoms	Emergency admission	Family history of beef allergy
1	17	F	Asthma, rhinitis, AD	6	P, U, A, H, W, D, N	30 min	+	–
2	7	M	Rhinitis	5	P, U, C, W, D	1 h	+	–
3	8	M	–	6	P, U	10 min	+	–
4	5	F	–	3	A, C, W, D, N, V	1 h	+	+
5	6	M	Asthma	3.5	U, A, C, D, N, AP	1 h	+	+
6	40	M	–	5	P, U, AP	1 h	+	+
7	9	M	Asthma	3	P, U, A, C, W, D, N, V, AP	15 min	+	+
8	11	F	Asthma, rhinitis	3	P, U, A, C, W, D, N, V, AP	15 min	+	+
9	36	M	–	3	P, U,	1 h	+	+
10	15	M	Rhinitis	1.5	P, U, A, H, C, W,	30 min	+	+
11	7	M	Asthma	4	P, U,	1 h	+	+
12	6	M	–	4	U, A	2 h	+	–

AD, atopic dermatitis; F, female; M, male.

A, angioedema; AP, abdominal pain; C, cough; D, dyspnoea; H, hoarseness; N, nausea; P, pruritus; U, urticaria; V, vomiting; W, wheezing.

Skin prick tests (SPTs)

The skin prick tests (SPTs) were performed on the volar side of the forearm with a commercially available beef extract (1 : 10 wt/vol.; Lot no. 7M 00449; Center Laboratories, Port Washington, NY), saline solution and histamine control (10 mg/ml) by using a bifurcated needle (Lincoln Diagnostics, Decatur, IL). A positive SPT response was defined as a wheal ≥ 3 mm larger than the negative control wheal. A prick-prick skin test (PPST) with raw and steam-cooked (10 min) beef was also performed as previously described (8). All tests were applied and measured by the same physician (F.O.). Two persons, one physician and one nurse, who did not have beef allergy, were used as negative controls to insure the validity of the PPST technique. As a routine procedure, all patients were also skin prick tested with common allergens (ALK, Allergologisk Laboratorium A/S, Hørsholm, Denmark) including house dust mites (*D. pteronyssinus* and *D. farinae*), pollens (grass, weed, and tree), moulds, animal dander (cat, dog, and horse), and foods (cow's milk, egg, peanut, wheat, fish, and soy).

Total and specific IgE

Serum total and specific IgE to beef were determined by CAP-FEIA, according to the manufacturer's instructions (Pharmacia-Upjohn, Uppsala, Sweden). A specific IgE level greater than 0.35 kU_A/l (class 1) was considered positive.

Food challenges

Food challenges were carried out at 8 AM, on the next day after the SPTs, in the pediatric allergy day ward. On arrival, a complete physical examination including vital signs (blood pressure, pulse, and respiratory rate) was performed, the emergency drug chart was completed, and an intravenous cannula was inserted.

Firstly, a labial food challenge (LFC) was performed, and all negative LFCs were followed by an open food challenge (OFC), except in the following situations: (i) last episode at least in the 12 months prior to the admittance; (ii) patients who have positive responses to at least two of the following tests: (a) SPT, (b) PPST with raw beef, (c) PPST with cooked beef, and (d) beef specific IgE

antibodies > 0.35 kU_A/l. Steam-cooked beef in home conditions was chopped into equal pieces (approximately 5 g) and was used for food challenges.

The technique described by Moneret-Vautrin (9) was used for LFC. Briefly, a piece of cooked beef was placed on the lower lip and left for 30 s to 2 min with the mouth slightly opened with a cotton swab between the lip and beef piece. The result was read 15 min later. Three types of symptom were taken as positive results in LFC: smoothing of the lip with disappearance of the fine physiological transversal wrinkles; oedema, presenting as local discoloration or a swelling of one or both lips; and, a contiguous rash, spreading in some cases as far as the neck.

Open food challenge (OFC) was performed by administering the pieces of cooked beef in a graded fashion. One piece of cooked beef (approximately 5 g) was administered at the beginning and the dose was then doubled every 20 min. The test was continued until the patient had convincing symptoms, or a total of approximately 75 g of cooked beef has been ingested (1 h). The convincing symptoms targeted with the OFC were defined as anaphylaxis, urticaria, angioedema, sneezing, rhinorrhoea, cough, wheezing, dyspnoea, abdominal pain, vomiting, and diarrhoea. Itching and nausea were not considered as convincing symptoms during or after challenge because of their subjective characteristics. Patients who were asymptomatic after the end of the challenge were observed for 4–6 h. The OFC (+) patients were observed for at least 12 h.

Results

The results of the beef allergy work-up are summarized in Table 2.

A total of three patients (two with commercial extract, and one with cooked beef) had positive skin test responses to beef. The PPSTs with raw beef were negative in all patients.

Six patients had positive SPT responses with our routine screening panel and most of them (4/6) were sensitized to house dust mites.

Table 2. Allergy work-up of the study group

Patient no.	Total IgE (kU/l)	Other sensitization	Prick test with beef (W/E)			Beef-specific IgE kU _A /l (class)	LFC	Clinical symptoms during OFC	Challenge dose (gm)
			Commercial	Raw	Cooked				
1	217	Mites, tree pollens	—	—	—	5.09 (3)	—	ND	—
2	437	Mites	6/10	—	—	36.6 (4)	—	ND	—
3	687	—	—	—	—	22.5 (4)	—	U	75
4	364	—	—	—	—	17.4 (3)	—	N, V, W	15
5	109	Moulds, weed pollens, dog dander	—	—	—	6.78 (3)	—	U	75
6	9	—	—	—	7/18	1.07 (2)	—	ND	—
7	269	—	—	—	—	5.68 (3)	+	ND	—
8	185	Mites	—	—	—	2.88 (2)	+	ND	—
9	3121	—	—	—	—	3.13 (2)	+	ND	—
10	375	Mites, dog dander, horse dander	4/10	—	—	8.89 (3)	+	ND	—
11	448	—	—	—	—	21.7 (4)	—	Negative	75
12	25	—	—	—	—	0.83 (2)	—	Negative	75

LFC, labial food challenge; OFC, oral food challenge; ND, not done; W/E, wheal/erythema. N, nausea; U, urticaria; V, vomiting; W, wheezing.

Ten (83%) patients had elevated serum IgE concentrations (median 316.5 kU/l, range 9–1321 kU/l) and beef-specific IgE was positive (class > 2) in all patients (median 6.23 kU_A/l, range 0.83–36.6 kU_A/l).

The LFC was positive in four (30%) patients. The positive LFC results were erythema under the lip in patients 7, 8 and 10, and swelling of the lower lip in patient 9. No systemic reaction occurred during LFC and all patients with (+) LFC were treated with oral hydroxyzine.

Of the six patients who fulfilled the criteria, OFC was performed on five patients. Patient 1 was not challenged because of the lack of parental consent.

Of the five OFC performed, three were positive; two patients tolerated the beef administered. Treatment with oral hydroxyzine was required in OFC positive cases. Nebulized salbutamol was administered to patient 4. No patients with a positive OFC needed epinephrine treatment for the reaction induced by the challenge test.

Interestingly, the rate of family history of beef allergy was 67% (8/12).

Discussion

In the present study, we performed detailed allergy work-up in 12 patients with convincing beef allergy history and found that the patients were from a certain region of the country and had a strong family history of beef allergy suggesting sensitization specific inheritance. Although SPTs are widely believed to be a sensitive method for detection of IgE mediated allergy, we found that this was not the case for beef allergy, and measurement of beef specific IgE appeared to be superior.

A possible explanation as to why the SPT results with commercial beef extract were negative in most of our patients may relate in part to the stability of the allergen. It is probable that certain specific allergens are lost during the manufacture of the extract.

Several studies have demonstrated the superiority of SPT and have proposed to perform SPT with fresh foods (10–13). It is also well known that cooking alters the reactivity of (2, 14), and reduces sensitization to beef (15). Nevertheless, we suggest that patients should be tested with food in the form that caused the reaction, and we performed PPSTs both with raw and cooked beef. The results were, however, negative in all patients with raw beef and in 11 patients with cooked beef. A speculative explanation might be that digestion in the gut may lead to the production of novel allergens that induce a specific IgE antibody response, allergens that are not found in the commercial beef extracts and beef itself, either raw or cooked. Although in our study, SPT did not appear sensitive enough to detect IgE-mediated beef allergy, we suggest that SPT should be performed with all three extracts (commercial, raw, and cooked) as the usual food allergy work-up.

The LFC is a simple, quick, cheap, and relatively safe method and is appealing for pediatric use in food allergy work-up. However, LFC was revealed to have a poor sensitivity (16), thus tending to justify the diagnosis of food allergy by oral challenge. The LFC was positive only in four patients in the present study.

The oral challenge test is the “gold standard” to confirm or refute histories of adverse reactions to foods when conducted in a double-blind, placebo-controlled manner (17). On the other hand, open challenge testing might be acceptable in young children or for screening the least suspected foods (18, 19), especially when the physician picked specific endpoints that were not subjective. Also, OFC is easy to perform, inexpensive, and not a time-intensive procedure when compared with double-blind, placebo-controlled food challenge. The patients in the present study reported convincing symptoms only after ingesting beef. All came from far distant cities to our clinic, in other words, we should offer quick-working procedures to make a proper diagnosis.

In general, oral challenge procedures are not suggested for patients who describe acute, life-threatening reactions (e.g. anaphylaxis). However, it is mentioned that a child with positive results on SPT but a doubtful history or a child with negative results on SPT should always be offered an open challenge (20). Obviously, to ensure optimal safety all challenge procedures should be undertaken in appropriately staffed and equipped units (21) and the minimum interval between the challenge and most recent reaction should be 1 or 2 years (20). Even though the histories were convincing, all patients who were challenged in our study had negative SPT and PPST, and had not been consuming beef at least during the last 2 years.

Our study demonstrates that beef-allergic patients can become tolerant. Since the study population is too small to perform adequate statistical analyzes, we are unable to conclude whether the type of reactions, or the age of the patient is a potential indicator of the possibility to become tolerant, however.

As beef and cow's milk contain bovine serum albumin, bovine gamma globulin, and other proteins in significant quantities, a higher prevalence of beef allergy might be expected among children allergic to cow's milk. Werfel et al. (2) reported that eight of the 11 children who reacted to beef (73%) were documented to be allergic to milk in previous double-blind, placebo-controlled food challenges. However, none of our patients reported allergic reactions to cow's milk ingestion, and none of them had positive SPT responses against cow's milk. Therefore, we did not screen cow's milk-specific IgE in the study population.

Although the sample size was small, our results revealed a familial tendency and a regional susceptibility

to beef allergy. It is known that the order of importance of specific allergens varies in different countries, which reflects the possible interaction of factors such as cultural and dietary habits, exposure to new allergenic products early in life, and genes. Hacettepe University Pediatric Allergy and Asthma Unit is not only one of the allergy outpatient clinics of Ankara, Turkey, but also a referral centre with a broad spectrum of patients from all regions of the country. Turkey is a large country and there are strict differences in dietary habits among peoples of different regions. Meat, in particular beef, is consumed in almost all meals in eastern and south-eastern Turkey. On the other hand, consumption of fish and other seafoods is frequent in the eastern Black Sea region. Thus, we would expect to see more fish and seafood allergies rather than beef allergy among peoples living in this region. Since consanguineous marriages are prevalent in the eastern Black Sea region, we should consider whether genetic factors play, at least in part, a role on beef allergy. This regional and familial tendency may resemble disorders like inborn errors of metabolism. However, type of symptoms, time of initial symptoms following the ingestion, high levels of total IgE, and positive specific IgE responses reveal an IgE-mediated allergic reaction rather than any other disorder.

We conclude that skin prick tests do not exclude IgE-mediated sensitization to beef. Thus, patients with suspected beef allergy should be screened additionally for beef-specific IgE antibodies. Since meat is an important source of protein, selected cases might be challenged under physician supervision in order to diagnose beef allergy, and to find out the cases who had developed tolerance.

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